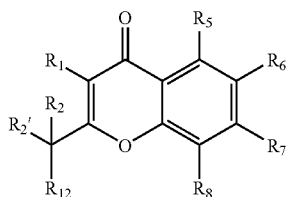


**[0096]** An object of the present invention is to develop inhibitors of mitotic kinesins, in particular KSP and especially human KSP, for the treatment of disorders associated with cell proliferation. Traditionally, dramatic improvements in the treatment of cancer, one type of cellular proliferative disorder, have been associated with identification of therapeutic agents acting through novel mechanisms. Examples of this include not only the taxane class of agents that appear to act on microtubule formation, but also the camptothecin class of topoisomerase I inhibitors. The compounds, compositions and methods described herein can differ in their selectivity and are preferably used to treat diseases of cellular proliferation, including, but not limited to cancer, hyperplasias, restenosis, cardiac hypertrophy, immune disorders, fungal disorders and inflammation.

**[0097]** Accordingly, the present invention relates to methods employing compounds represented by Formula



Formula I

wherein:

**[0098]**  $R_1$  is chosen from hydrogen, optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, and optionally substituted heteroaralkyl-;

**[0099]**  $R_2$  and  $R_{2'}$  are independently chosen from hydrogen, optionally substituted optionally substituted alkoxy, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, and optionally substituted heteroaralkyl-; or  $R_2$  and  $R_{2'}$  taken together form an optionally substituted 3- to 7-membered ring;

**[0100]**  $R_{12}$  is selected from the group consisting of optionally substituted imidazolyl, optionally substituted imidazolynyl,  $-NHR_4$ ;  $-N(R_4)(COR_3)$ ;  $LN(R_4)(SO_2R_{3a})$ ; and  $-N(R_4)(CH_2R_{3b})$ ;

**[0101]**  $R_3$  is chosen from hydrogen, optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, optionally substituted heteroaralkyl-,  $R_{15}O-$  and  $R_{17}NH-$ ;

**[0102]**  $R_{3a}$  is chosen from optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, optionally substituted heteroaralkyl-, and  $R_{17}NH-$ ;

**[0103]**  $R_{3b}$  is chosen from hydrogen, optionally substituted alkyl-, optionally substituted aryl, optionally substituted aralkyl-, optionally substituted heteroaryl-, and optionally substituted heteroaralkyl-;

**[0104]**  $R_4$  is chosen from hydrogen, optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heterocyclyl-, and optionally substituted heteroaralkyl-;

**[0105]**  $R_5$ ,  $R_6$ ,  $R_7$  and  $R_8$  are independently chosen from hydrogen, acyl, optionally substituted alkyl-, optionally substituted alkoxy, halogen, hydroxyl, nitro, cyano, dialkylamino, alkylsulfonyl-, alkylsulfonamido-, alkylthio-, car-

boxyalkyl-, carboxamido-, aminocarbonyl-, optionally substituted aryl and optionally substituted heteroaryl-;

**[0106]**  $R_{15}$  is chosen from optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, and optionally substituted heteroaralkyl-, and

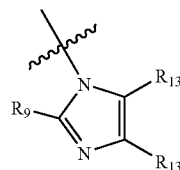
**[0107]**  $R_{17}$  is hydrogen, optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, or optionally substituted heteroaralkyl-, including single stereoisomers, mixtures of stereoisomers:

**[0108]** a pharmaceutically acceptable salt of a compound of Formula I;

**[0109]** a pharmaceutically acceptable solvate of a pharmaceutically acceptable solvate of a compound of Formula I;

**[0110]** or a pharmaceutically acceptable solvate of a pharmaceutically acceptable salt of a compound of Formula I.

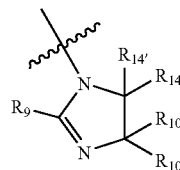
**[0111]** When  $R_{12}$  is an imidazole,  $R_{12}$  has the formula:



wherein

**[0112]**  $R_9$  is chosen from hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aryl- $C_1$ - $C_4$ -alkyl-, optionally substituted heteroaryl- $C_1$ - $C_4$ -alkyl optionally substituted aryl- $C_1$ - $C_4$ -alkoxy-, optionally substituted heteroaryl- $C_1$ - $C_4$ -alkoxy optionally substituted heteroaryl-, and  $R_{13}$  and  $R_{13'}$  are independently hydrogen, optionally substituted  $C_1$ - $C_8$  alkyl, optionally substituted aryl, or optionally substituted aryl- $C_1$ - $C_4$ -alkyl-.

**[0113]** When  $R_{12}$  is an imidazoline,  $R_{12}$  has the formula



**[0114]** wherein

**[0115]**  $R_9$  is chosen from hydrogen, optionally substituted  $C_1$ - $C_8$  optionally substituted aryl, optionally substituted aryl- $C_1$ - $C_4$ -alkyl-, and optionally substituted heteroaryl-; and  $R_{10}$ ,  $R_{14}$ , and  $R_{14'}$  are independently chosen from hydrogen, optionally substituted  $C_1$ - $C_8$  alkyl, optionally substituted aryl, and optionally substituted aryl- $C_1$ - $C_4$ -alkyl-.

**[0116]** In one embodiment,  $R_1$  is chosen from hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heteroaralkyl-;

**[0117]**  $R_2$  and  $R_{2'}$  are independently chosen from hydrogen, optionally substituted alkyl, optionally substituted alkoxy, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heteroaralkyl-; or  $R_2$  and  $R_{2'}$  taken together form an